

Hydrogen Sulfide Ameliorates Developmental Impairments of Rat Offspring with Prenatal Hyperhomocysteinemia

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Abstract

Maternal high levels of the redox active amino acid homocysteine-called hyperhomocysteinemia (hHCY)-can affect the health state of the progeny. The effects of hydrogen sulfide (H₂S) treatment on rats with maternal hHCY remain unknown. In the present study, we characterized the physical development, reflex ontogeny, locomotion and exploratory activity, muscle strength, motor coordination, and brain redox state of pups with maternal hHCY and tested potential beneficial action of the H₂S donor-sodium hydrosulfide (NaHS)-on these parameters. Our results indicate a significant decrease in litter size and body weight of pups from dams fed with methionine-rich diet. In hHCY pups, a delay in the formation of sensory-motor reflexes was observed. Locomotor activity tested in the open field by head rearings, crossed squares, and rearings of hHCY pups at all studied ages (P8, P16, and P26) was diminished. Exploratory activity was decreased, and emotionality was higher in rats with hHCY. Prenatal hHCY resulted in reduced muscle strength and motor coordination assessed by the paw grip endurance test and rotarod test. Remarkably, administration of NaHS to pregnant rats with hHCY prevented the observed deleterious effects of high homocysteine on fetus development. In rats with prenatal hHCY, the endogenous generation of H₂S brain tissues was lower compared to control and NaHS administration restored the H₂S level to control values. Moreover, using redox signaling assays, we found an increased level of malondialdehyde (MDA), the end product of lipid peroxidation, and decreased activity of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) in the brain tissues of rats of the hHCY group. Notably, NaHS treatment restored the level of MDA and the activity of SOD and GPx. Our data suggest that H₂S has neuroprotective/antioxidant effects against homocysteine-induced neurotoxicity providing a potential strategy for the prevention of developmental impairments in newborns.

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